

Single Stranded DNA Induced Assembly of Gold Nanoparticles

Jun Yang,^a Jim Yang Lee,^{*a,b} T. C. Deivaraj,^b and Heng-Phon Too^c

^a Department of Chemical and Environmental Engineering, National University of Singapore, 10 Kent Ridge Crescent, Singapore 119260. Fax: 65 6779 1936; Tel: 65 6874 2899; E-mail: cheleejy@nus.edu.sg

^b Singapore-MIT Alliance, 4 Engineering Drive 3, National University of Singapore, Singapore 117576.

^c Department of Biochemistry, National University of Singapore, 10 Kent Ridge Crescent, Singapore 119260.

Abstract — The binding affinity of single stranded DNA (ssDNA) for gold nanoparticle surface is studied in this work. The data indicate that the strength of interaction between ssDNA and Au particle surface is closely related to the particle size, with smaller particles (5 nm) producing the most pronounced effects. From these experimental findings, a single stranded DNA (ssDNA) based method to assimilate 13 and 5 nm gold nanoparticles was developed, and verified by transmission electron microscopy (TEM).

Index Terms—Self assembly, gold nanoparticles, DNA, oligonucleotides.

I. INTRODUCTION

Lately DNA guided assembly of metal nanoparticles has been increasingly used for DNA diagnostics, and for generating interesting nanostructured materials[1],[2]. There are no lack of reports on the application of this technique to organize metal nanoparticles into one-, two-

or three-dimensional arrays[3]-[23]. Mirkin's group, in particular, has developed protocols to assemble Au nanoparticles based on site-selective hybridization, the cornerstone of the molecular recognition properties of DNA[4], [8],[16],[18],[23]. In Mirkin's method, Au nanoparticles are first functionalized by oligonucleotides terminated with alkanethiol groups at the 3' or 5' position. Two non-complementary nucleotide sequences are used to prepare two distinct groups of gold nanoparticles. Particle linking between the groups occurs by adding duplex DNA with sticky ends that are complementary to the nucleotide sequences on the Au particles. A macroscopic network of particles held together by the duplex DNA interconnects is formed as a result. Aggregated 13 nm [4], [16], [18], 31 nm and 50 nm Au nanoparticles [23] and binary nanoparticle networks containing 8 and 31 nm Au nanoparticles [8] have been successfully assimilated this way. However, difficulties arose when we tried to assemble smaller Au nanoparticles (5 nm) using this procedure. No hybridization was detected when duplex DNA with sticky ends complementary to the nucleotide sequences on the 5 nm Au particles was added. Further investigations suggested the presence of strong interactions between the oligonucleotide backbone and the surface of small gold nanoparticles. Additionally, small Au nanoparticles could be stabilized by single stranded DNA (ssDNA) without any modification at the 3' or 5' ends of the latter. The stability of the ssDNA-Au nanocomposite is not a strong function of the nucleotide sequence in the ssDNA.

Based on the finding that smaller Au nanoparticles could be stabilized by ssDNA, a new protocol was developed to allow the successful assembly of ssDNA-functionalized 5 and 13 nm Au nanoparticles. The proof-of-concept demonstrations reported herein suggest that this technique can be extended to multicomponent systems where nanoparticles with different chemical composition or size

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Jun Yang is with the Department of Chemical and Environmental Engineering, National University of Singapore, Singapore-119260 (engp2422@nus.edu.sg).

Jim Yang Lee is with Department of Chemical and Environmental Engineering, National University of Singapore, Singapore-119260 and also a Fellow, Singapore-MIT Alliance, National University of Singapore, Singapore-117576. (phone: 65-6874-2899; fax: 65-6779-1936; e-mail: cheleejy@nus.edu.sg).

T. C. Deivaraj is with the Singapore-MIT Alliance, National University of Singapore, Singapore-117576. (e-mail: smatcd@nus.edu.sg).

Heng-Phon Too is with Department of Biochemistry, National University of Singapore, Singapore-119260 and also a Fellow, Singapore-MIT Alliance, National University of Singapore, Singapore-117576. (e-mail: bchtoohp@nus.edu.sg).

may be assimilated based on their interactions with ssDNA. The results in this work also highlight the potential pitfall in using DNA melting point analysis to infer the aggregation of small Au nanoparticles by DNA hybridization.

II. EXPERIMENTAL

A. General description

Hydrogen tetrachloroaurate(III) trihydrate, $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$ (99.9%), was purchased from Aldrich (Milwaukee, WI, USA). Sodium borohydride, NaBH_4 (98%) was from Ajax (Alburn, Australia). Sodium citrate dihydrate, $\text{C}_6\text{H}_5\text{Na}_3\text{O}_7 \cdot 2\text{H}_2\text{O}$ (98%), was from MERCK (Darmstadt, Germany). The thiolated single stranded DNA, abbreviated HS-ssDNA, and supplied by Prologo Singapore, is a 20-base oligonucleotide with the following sequence: 5'-HS-(CH₂)₆-TAT TCT TAT TAG TAT GAT CT-3'. Single stranded DNA, abbreviated ssDNA, having the same nucleotide sequence as HS-ssDNA but without the HS-(CH₂)₆- attachment at the 5' end, was also supplied by Prologo. All chemicals were used as received. Water was purified by a Milli-Q water purification system. All glassware and Teflon-coated magnetic stir bars were cleaned with *aqua regia*, followed by copious rinsing with distilled water and drying in oven. Transmission electron microscopy (TEM) using a JEOL JEM2010 system operating at 200kV was used to size the particles. For TEM measurements a drop of the nanoparticle solution was placed on a 3mm copper grid covered with a continuous carbon film. Excess solution was removed by an adsorbent paper and the sample was dried under vacuum at room temperature. UV-visible spectroscopic measurements of the Au nanoparticle solution were carried out on a Shimadzu UV-2450 spectrophotometer.

B. Preparation of Au nanoparticles

Approximately 13 nm Au nanoparticles were prepared by the citrate reduction of HAuCl_4 [24],[25]. An aqueous solution of HAuCl_4 (1 mM, 20 mL) was refluxed at 110°C with stirring in an oil bath. 2 mL of a 38.8 mM aqueous tri-sodium citrate solution was added quickly, which resulted in a series of color change before finally arriving at a wine red solution. The mixture was refluxed for another 15 minutes and allowed to cool to room temperature. The 5 nm Au nanoparticles encapsulated with citrate shells were prepared by a slightly different procedure. Briefly, 10mL of 1 mM aqueous solution of HAuCl_4 was mixed with 0.8 mL of 38.8 mM aqueous sodium citrate solution used as a stabilizer. 0.3 mL of 100 mM aqueous solution of NaBH_4 was then added dropwise under vigorous stirring, giving rise to a red colored Au hydrosol. The Au hydrosol was only used after ageing for 24 hours to decompose residual NaBH_4 .

C. Preparation of ssDNA stabilized Au nanoparticles

Au nanoparticles stabilized by ssDNA were prepared by adding 25 μL ssDNA solution containing 0.5 nmol of

ssDNA to 200 μL of an aqueous 5 nm Au nanoparticle solution (~260 nM) or 200 μL of aqueous 13 nm Au particle solution (~17 nM). The mixture was then aged for more than 3 hours. The effect of the (molar) ratio of ssDNA to Au particles on the stability of ssDNA stabilized Au nanoparticles was investigated by varying the amount of ssDNA solution (20 μM) used.

D. Preparation of HS-ssDNA stabilized 13 nm Au nanoparticles

13 nm Au nanoparticles stabilized by HS-ssDNA were obtained by the Mirkin's procedure [18],[26]. To 200 μL of an aqueous 13 nm Au nanoparticle solution (~17 nM), 25 μL of 20 μM HS-ssDNA solution was added. After standing for 16 hours, the solution was mixed with 25 μL 1M PBS buffer (1M NaCl, 100 mM phosphate buffer, pH = 7) and allowed to stand for 40 hours.

E. Assembly of 13 and 5 nm Au particles by HS-ssDNA.

After aging, the solution of HS-ssDNA stabilized 13 nm Au nanoparticles was centrifuged for 30 minutes at 15000 rpm to remove the excess reagents. The red oily pellets remained after the removal of supernatant were washed with 5 mL of deionized water, recentrifuged, and dispersed in 200 μL of 5 nm Au particle solution. Aggregates of 13 and 5 nm Au nanoparticles assembled by HS-ssDNA were formed 3~4 hours later.

III. RESULTS AND DISCUSSION

A. Stability of ssDNA stabilized 5 nm Au nanoparticles

In the absence of ssDNA, the Au nanoparticle solution was not stable in a NaCl solution. Color change from red to blue occurred immediately after contacting the Au nanoparticle solution with a 0.1 M PBS buffer, signaling the aggregation of the nanoparticles in the solution. However, for a mixture of 5 nm Au nanoparticle solution and ssDNA solution which had been aged for 3 hours, the addition of PBS buffer was unable to bring about the color change, suggesting that the Au nanoparticle were protected by ssDNA. The ssDNA protected Au nanoparticles were

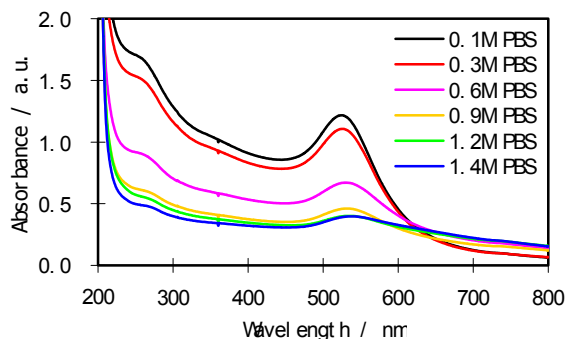
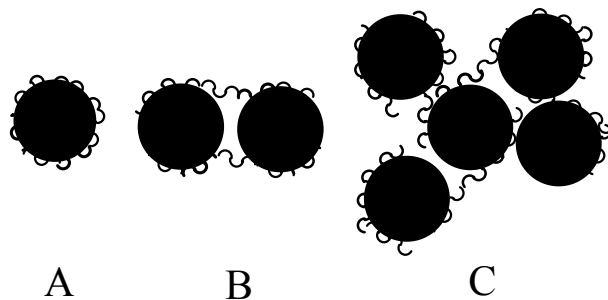


Fig. 1. UV-visible spectra of ssDNA stabilized Au nanoparticle aged in PBS buffer of different concentrations for 16 hours.

stable in salt solutions of even higher concentrations and temperature.

Figure 1 shows the UV-visible spectra of ssDNA stabilized Au nanoparticle aged in PBS buffer of different concentrations for 16 hours. Measurable changes in the frequency and the intensity of the Au surface plasmon band were only detected when the concentration of the PBS buffer had reached 0.6 M, as shown by the red-shift from 523 nm to 534 nm. Increasing the solution temperature up to 70°C also failed to destabilize the ssDNA protected 5 nm Au nanoparticles.

It is possible that the Au nanoparticles interacted with ssDNA by coordinating with the nitrogen bases in the nucleosides. Interaction of this nature has been suggested by Herne, et al [27] for gold film and by Mirkin's group [26] for 16 nm Au nanoparticles. However, interaction as strong as that between the 5 nm Au nanoparticles and ssDNA was not expected, and its strong dependence on particle size has not been reported. Equally important is the apparent lack of correlation between the interaction and the nucleotide sequence in the ssDNA. The observation is significantly different from the results of Storhoff and coworkers,[26] who found that the stability of DNA stabilized 16 nm gold nanoparticles was dependent on the DNA base sequence. The difference is used to infer a strong and undifferentiated affinity between the nitrogen bases and the surface atoms of the smaller Au nanoparticle. Beside the base sequence described in the experimental section, we have also used sequences such as 5'-TAT TGC TTT TAA GTA TAT AA-3', 5'-ATG GCA ACT ATA CGC GCT AG-3' and 5'-AAA CGA CTC TAG CGC GTA TA-3'. In both cases the stability of the ssDNA stabilized 5 nm Au nanoparticles was similar to the results in Figure 1.



Scheme 1. Possible aggregate structures formed by ssDNA stabilized 5 nm Au particles in a colloidal solution.

The high stability of ssDNA protected Au nanoparticles may be explained by the creation of a number of model structures in the solution such as those shown in Scheme 1. These proposed structures are more than hypothetical as they suggest the formation of geometrically distinct aggregates that can be detected by analytical TEM. The TEM image of ssDNA stabilized 5 nm Au nanoparticles (Figure 2) confirms such expectation. As a control, the TEM image of citrate stabilized 5 nm Au nanoparticles

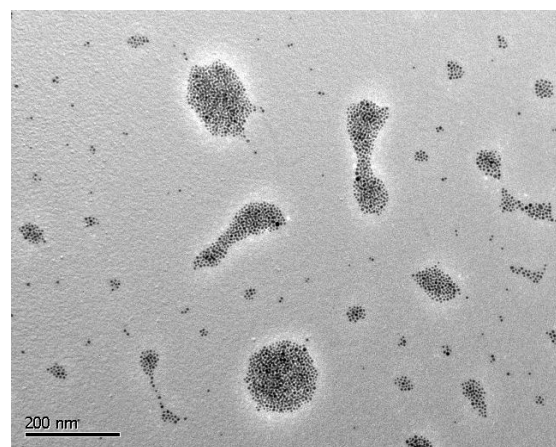


Fig. 2. TEM image of ssDNA stabilized 5 nm Au nanoparticles.

without ssDNA was also taken (Figure 3). The lack of extended aggregates in the latter is fairly obvious by comparison.

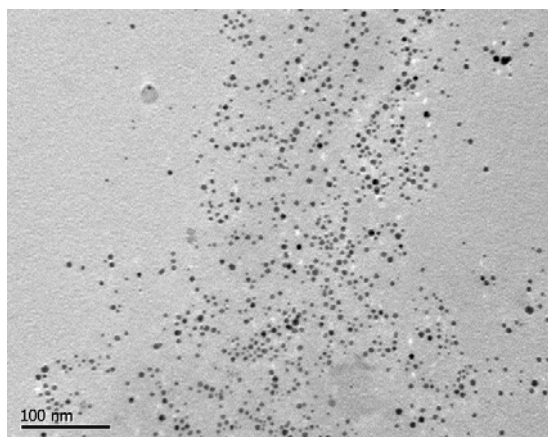
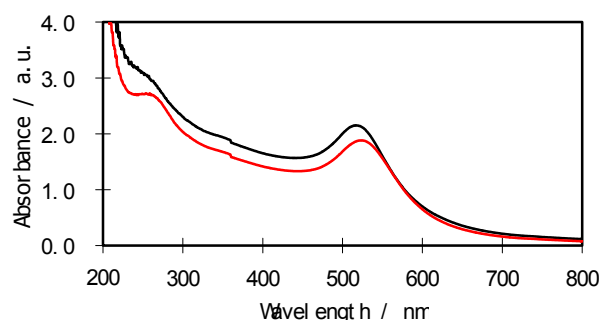


Fig. 3. TEM image of citrate stabilized 5 nm Au nanoparticles (no ssDNA).



The UV-visible spectra of citrate-stabilized 5 nm Au nanoparticles and ssDNA-stabilized 5 nm Au nanoparticles in aqueous solutions are shown in Figure 4. There was a modest red-shift in the surface plasmon band from 517 to 523 nm after the ssDNA stabilization of the

gold nanoparticles, which corresponds well with some extent of Au particle aggregation in the solution.

Varying the molar ratio of ssDNA to 5 nm Au particles

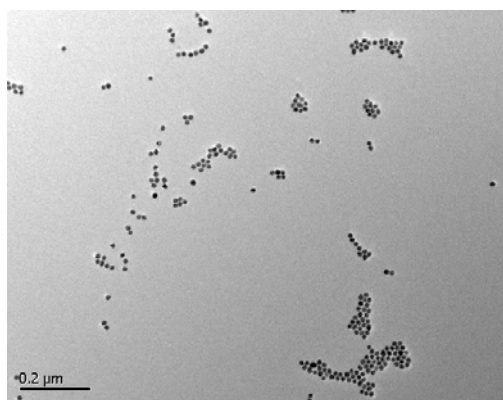


Fig. 5. TEM image of ssDNA stabilized 13 nm Au nanoparticles.

from 20 to 150 had negligible effect on the stability of the ssDNA stabilized Au nanoparticles. This is taken to suggest that the attachment of ssDNA to the surface of the 5 nm Au nanoparticles could reach the saturation level easily.

The interaction between ssDNA and Au nanoparticle surface was strongly affected by the particle size. In addition to the 5nm Au nanoparticles, we have also investigated the stability of ssDNA stabilized 13 nm Au nanoparticles. While some Au particle aggregation can be found in the TEM image of Figure 5, the extent of aggregation and the aggregate size are significantly smaller

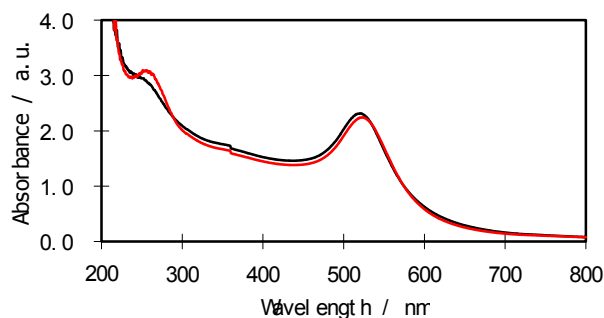


Fig. 6. UV-visible spectra for citrate stabilized (black line) and ssDNA stabilized 13 nm Au nanoparticles in aqueous solutions (red line).

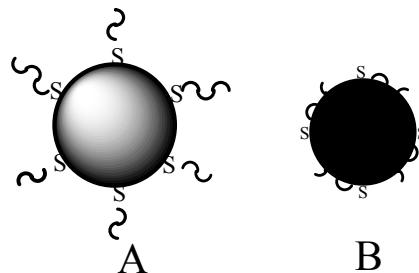
than that of ssDNA stabilized 5 nm Au nanoparticles.

A mere 4 nm red-shift (from 520 to 524) in the UV-visible spectra (Figure 6) further corroborated the limited aggregation in 13nm Au particles. However, the same small red-shift was referred to as the influence of surface modification, centrifugation and electrolyte in Mirkin's work[18]. The stability of ssDNA stabilized 13 nm Au particles was rather weak, and color change from red to purple to blue would occur several minutes after the addition of a 0.1 M PBS solution. However, without the ssDNA, the color change of citrate stabilized 13nm Au nanoparticles from red to blue would occur even faster and with more dilute PBS solutions. These results clearly

showed that ssDNA could interact with Au nanoparticles of any size, and the interaction would increase with decreasing particle size.

B Assembly of 13 and 5 nm Au particles by HS-ssDNA.

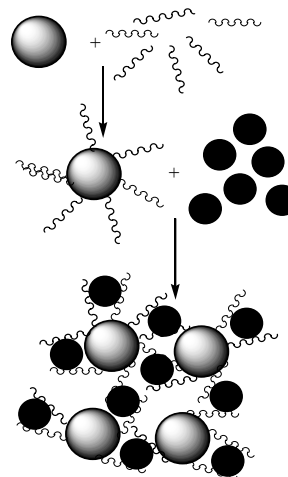
When HS-ssDNA is added to a solution of Au



Scheme 2. (A) Weak interaction between oligonucleotide and gold particle surface; (B) Strong interaction between oligonucleotide and gold particle surface.

nanoparticles, it is generally believed that the thiol end of the oligonucleotide would bind preferentially and covalently to the Au surface[28],[29]. However, the actual oligonucleotide binding model (Scheme 2) may differ depending on the strength of interaction between the oligonucleotide and the nanoparticle surface, which is determined by particle size from the discussions in the previous section.

The same conclusion excepting the particle size effect



Scheme 3. Aggregates of 13 and 5 nm Au particles assembled by HS-ssDNA.

was also obtained by Mirkin *et al* [26] in their investigation of the interaction between different deoxynucleosides and 16 nm Au nanoparticles. Scheme 2A and Scheme 2B should therefore reflect the two prevailing binding types of HS-ssDNA on the surface of 13 nm and 5 nm Au nanoparticles respectively. The wrapping around of oligonucleotides on the 5nm Au particle surface explains why the Mirkin's site selective procedure would not work for smaller Au nanoparticles. However, we could still assemble 13 nm and 5 nm Au particles with a single stranded DNA based on the mechanism shown in Scheme

3. Here the extended oligonucleotides on the 13 nm particles were used to bridge the smaller, and citrate protected 5 nm particles. Experimentally this was accomplished by dispersing the HS-ssDNA stabilized 13 nm Au nanoparticles in a solution of 5 nm citrate protected Au particles. After aging the mixture of HS-ssDNA stabilized 13 nm Au particles and 5 nm citrate stabilized Au particles for more than 3 hours, the color of the mixture changed from red to purple, indicating the assembly of 13 and 5 nm Au particles, where the 5 nm Au nanoparticles served as interconnects to integrate the 13 nm Au particles using the extended HS-ssDNA. The assembly also produced a red shift in the surface plasmon resonance (SPR) band of Au nanoparticles from 522 nm to 533 nm (Figure 7). It should be reiterated that neither the HS-ssDNA stabilized 15 nm Au particles (Figure 8) nor the

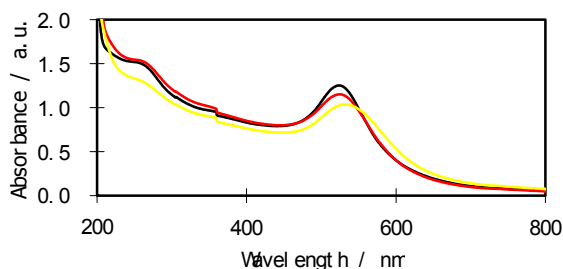


Fig. 7. UV-visible spectra of HS-ssDNA stabilized Au particles (black line), mixture of 13 and 5 nm citrate stabilized Au nanoparticles (red line) and aggregates of 13 and 5 nm Au assembled by HS-ssDNA in aqueous solutions (yellow line).

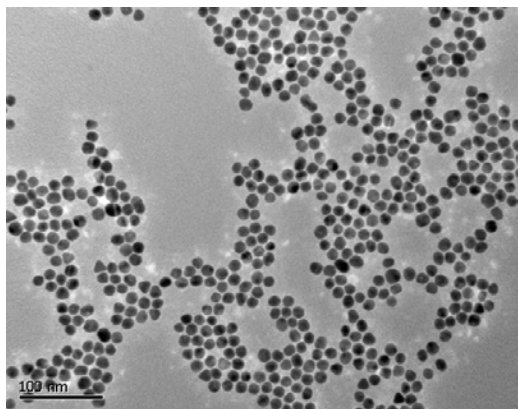


Fig. 8. TEM image of HS-ssDNA stabilized 13 nm Au nanoparticles.

citrate protected 5 nm Au particles (Figure 3) would aggregate under the same experimental conditions.

TEM imaging (Figure 9) also showed some extended aggregates formed by the two different sized Au particles with good repeatability. The gold particles formed two principal structures on the copper TEM grid: three-dimensional assemblies or “satellite structures” consisting of 13 nm Au nanoparticles surrounded by many 5 nm Au nanoparticles. Almost no isolated particles were found on the TEM grid.

As a control, the TEM image of a mixture of 13 and 5 nm citrate stabilized Au nanoparticles (no ssDNA) was

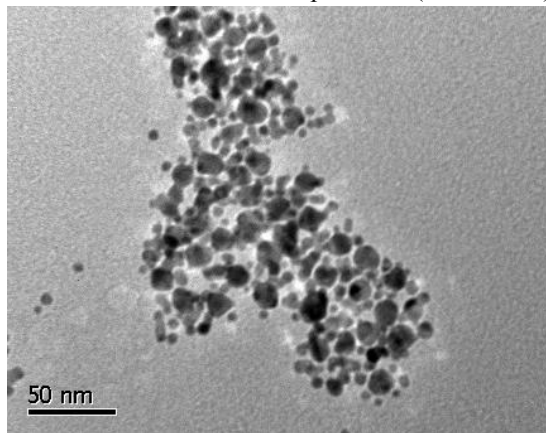


Fig. 9. TEM images of the aggregates of 13 and 5 nm Au particles.

taken and is shown in Figure 10. Figure 10 shows mostly randomly dispersed particles or aggregates consisting of particles of same size. The lack of any correlation patterns between the particles accentuates the difference between this Figure and Figure 9. In addition, there was no color change in the mixture of 13 and 5 nm citrate stabilized Au colloidal solution after several days of ageing. There was also no red shift in the Au SPR band in the mixture of 13 and 5 nm citrate stabilized Au colloidal solution (red line in Figure 7).

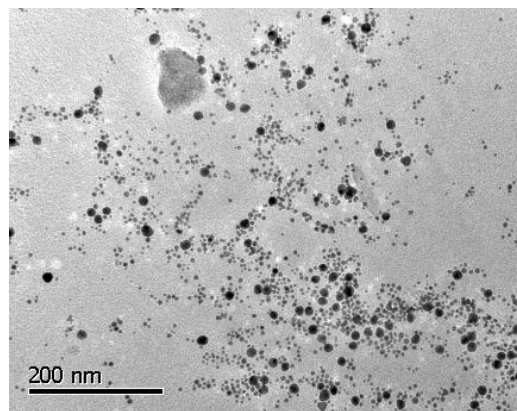


Fig. 10. TEM image of a mixture of 13 and 5 nm citrate stabilized Au nanoparticles.

The proof-of-concept demonstrations given here should be extendable to more complex systems, e.g. the assembly of a multicomponent system from nanoparticles with different chemical compositions and/or size. This work also cautions against the over-reliance on DNA melting point analysis to infer the mechanism of nanoparticle assembly in hybridization experiments involving a linker. This is particularly so for systems containing small Au nanoparticles. In such systems the melting point only reflects the properties of the DNA linker while the particles may be linked by ssDNA, and this may lead to some gross misinterpretation of the experimental data.

IV. CONCLUSIONS

This article shows how single stranded DNA (ssDNA) could be used without a complementary sequence to direct the placement of two different sized Au nanoparticles (13 and 5 nm) in an extended particle assembly. Although only two different sized metal nanoparticles were used as an example, there is no reason why this technique could not be extended to the assembly of other nanoscale building blocks including particles of different chemical compositions (e.g., Ag, Ru, Pt, Au). We believe that such a ssDNA guided assembly of nanoparticles is useful to materials scientists to produce new composites with interesting properties that may not be obtainable in other ways.

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